REMARKS

This application is amended in a manner believed to place it in condition for allowance at the time of the next Official Action.

Claims 9, 10, 13 and 15 are amended.

Claims 16-19 are new.

Support for the amended and new claims may be found generally throughout the present specification, particularly at page 3, line 4 to page 4, line 20 and page 7, line 11 to page 8, line 4.

Claims 3-6 and 12 are cancelled without prejudice.

Claims 1, 2, 7-10 and 13-19 remain pending in the application.

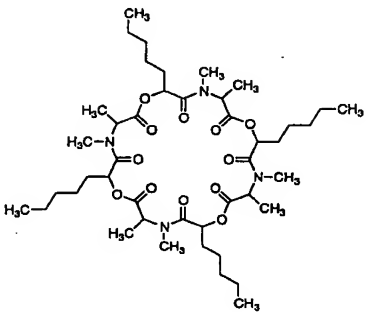
Claim 2 is withdrawn from further consideration as being directed to a non-elected invention.

The Official Action objected to the present specification for being replete with terms which are not clear, concise, and exact. The Official Action stated that the specification should be revised, particularly pages 1, 2 and 4.

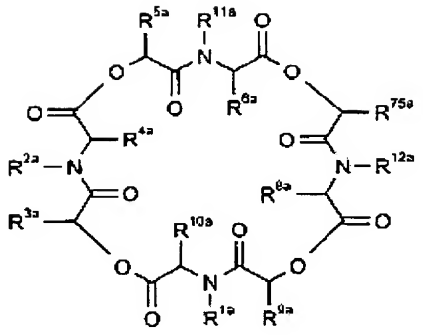
The present specification at pages 1-4 is amended. It is believed that no new matter has been introduced into the present specification, and that the present specification is now clear, concise, and exact. However, applicants welcome any further suggestions that would help to clarify the present specification.

Claims 1, 7-10 and 13-15 were rejected under 35 U.S.C. 102(b) as being anticipated by KALBE et al. WO 01/62268 A1 (KALBE '268). Applicants respectfully disagree.

The present claims are directed to the substance FKI-1033, which may be isolated from a cultured mass of a microorganism belonging to the *Verticillium* genus of fungi, and compositions comprising the substance FKI-1033. The substance FKI-1033 has a molecular weight of 875.5397 and is represented by the formula:



KALBE '268 very broadly discloses a generic depsipeptide formula that may include anywhere from 6 to 30 ring or chain atoms, preferably 18-24 ring atoms, and, in particular, 24 ring atoms as described by formula Ia (e.g. as disclosed in the U.S. equivalent US 2003/0125244 A1 at paragraphs 19 and 20):



(Ia)

Formula Ia resembles the formula of FKI-1033 when R^{1a}, R^{2a}, R^{4a}, R^{6a}, R^{8a}, R^{10a}, R^{11a} and R^{12a} are methyl groups and R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a} are n-pentyl groups.

However, a generic formula which encompasses a vast number of compounds does not describe and thus anticipate all compounds embraced there in merely because they are within the scope of the formula. *In re Petering et al.* (CCPA 1964) 301 F.2d 676, 133 USPQ 275; *E.I. DuPont de Nemours & Co. v. Ladd, Comr. Pats., et al.* (CADC 1964) 328 F.2d 547, 140 USPQ 297. There can be no anticipation where the reference is so broad that the likelihood of arriving at the claimed composition would be the same as discovering the combination of a safe by an inspection of its dials, *Ex parte Garvey* (POBA 1939) 41 USPQ 583; *Ex parte Starr* (POBA 1938) 44 USPQ 545, nor is anticipation made out by a hindsight selection based on an applicant's disclosure of variables of a broad generic disclosure. *In re Ruschig et al.* (CCPA 1965) 343 F.2d 965, 145 USPQ 274.

Indeed, formula Ia encompasses such a vast number of structures that arriving at the formula for substance FKI-1033

would only be possible by hindsight selection. Even in a preferred embodiment of formula Ia, KALBE '268 discloses no fewer than 2401 possible combinations for the group of R^{1a}, R^{2a}, R^{11a}, and R^{12a} (i.e. independently of one another, one of methyl, ethyl, propyl, isopropyl , n-butyl, s-butyl, and t-butyl in paragraphs 64 and 65 of U.S. equivalent US 2003/0125244 A1). As for the group of R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a} and the group of R^{4a}, R^{6a}, R^{8a} and R^{10a}, the number of possible combinations is magnitudes greater than the number of the combinations of R^{1a}, R^{2a}, R^{11a}, and R^{12a} (i.e. paragraphs 66 and 67 of U.S. equivalent US 2003/0125244 A1).

Moreover, KALBE '268 fails to disclose or even suggest that formula Ia may be isolated from a cultured mass of a microorganism having ability to produce the FKI-1033 substance and belonging to the *Verticillium* genus of fungi, as recited in claims 15-19, and that formula Ia has ryanodine binding inhibition activity or is part of a composition having ryanodine binding inhibition activity, as recited in claims 7, 9, 10 and 13-15.

Thus, the disclosure of KALBE '268 lacks the specificity required for a finding of anticipation, and KALBE '268 does not anticipate claims 1, 7-10, 13-15, and new claims 16-19.

Therefore, applicants respectfully request that the anticipation rejection be withdrawn.

KALBE '268 also fails to render obvious the claims. KALBE '268 does not suggest including any particular structure represented by the generic formula Ia in compositions having ryanodine binding inhibition activity, nor does KALBE '268 suggest isolating formula Ia from a culture comprising a microorganism belonging to the *Verticillium* genus of fungi. Thus, as KALBE '268 fails to even recognize the particular uses for the substance FKI-1033 or the particular microorganism that produces substance FKI-1033 as recited, there would be no motivation for modifying KALBE '286 so as to limit formula Ia to having a methyl group for R^{1a}, R^{2a}, R^{4a}, R^{6a}, R^{8a}, R^{10a}, R^{11a} and R^{12a} and an n-pentyl group for R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a} so as to resemble the recited substance FKI-1033.

Furthermore, KALBE '268 does not even appear interested in compounds having a molecular weight similar to substance FKI-1033. KALBE '268 is directed to the discovery that depsipeptides having molecular weights greater than 1000u possess pharmaceutical activity (e.g. paragraph 11 of the U.S. equivalent US 2003/0125244 A1). Substance FKI-1033 of the present invention has a molecular weight of 875.5397, as discussed above. Thus, there would be no motivation to select a methyl group for R^{1a}, R^{2a}, R^{4a}, R^{6a}, R^{8a}, R^{10a}, R^{11a} and R^{12a} and an n-pentyl group for R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a}, as the resulting molecular weight would be lower than the molecular weight of interest disclosed by KALBE '268.

Moreover, while KALBE '268 discloses that the 24-ring cyclic depsipeptides have good endoparasiticidal activities, KALBE '268 fails to recognize the superior unexpected ectoparasiticidal (anthropodicidal) activities. The substance FKI-1033 has special unexpected activity, as described in the Declaration filed under 37 C.F.R. 1.132 filed with this amendment.

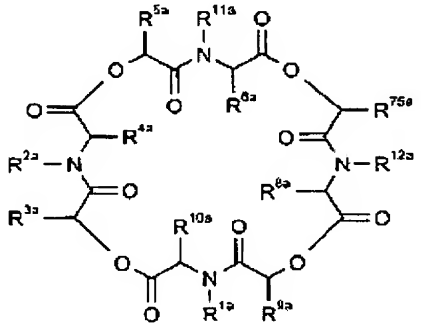
In the declaration, the toxicity of FKI-1033 was compared to emodepside against adult cattle ticks. Emodepside is "particularly preferred" by KALBE '268 (e.g. paragraph 48 of the U.S. equivalent US 2003/0125244 A1, or page 12, lines 9-10 of the WO document). In emersion tests, FKI-1033 killed 100% of ticks at 20 µg/ml, but emodepside did not kill any ticks at 100 µg/ml. In injection tests, FKI-1033 killed 100% of the ticks at 0.16 µg/ml, and emodepside killed 100% of the ticks at 20 µg/ml. Thus, FKI-1033 proved to be far more potent than Emodepside in anthropodicidal activity (See Item 1 of the declaration).

KALBE '268 also fails to recognize depsipeptides that would have a ryanodine binding inhibition activity. FKI-1033 unexpectedly showed 50% ryanodine binding inhibition activity against the American cockroach ryanodine receptor at 4.2 µM, and all tested 24 ring cyclic depsipeptides (bassianolide and PF1022A, or PF 1022 as disclosed by KALBE) and 18-ring cyclic depsipeptides (enniatin A and beauvericin) showed no binding inhibition at 110 µM (Item 2 of the declaration).

Therefore, in view of the above, applicants believe the claims are neither anticipated nor rendered obvious by KALBE '286.

Claims 1, 7-10 and 13-15 were rejected under 35 U.S.C. 102(a) as being anticipated by KALBE et al. WO 02/00202 A1 (KALBE '202). Applicants respectfully disagree.

The disclosure of KALBE '202 is similar to the disclosure of KALBE '268. KALBE '202 also broadly discloses a generic depsipeptide formula that may include anywhere from 6 to 30 ring or chain atoms, and, in particular, 24 ring atoms formula Ia (e.g. the U.S. equivalent US 2004/0043925 A1 at paragraphs 18, 19 and 52):



(Ia)

Formula Ia resembles substance FKI-1033 when R^{1a}, R^{2a}, R^{4a}, R^{6a}, R^{8a}, R^{10a}, R^{11a} and R^{12a} are methyl groups and R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a} are n-pentyl groups.

However, a generic formula which encompasses a vast number of compounds does not describe and thus anticipate all compounds embraced there in merely because they are within the scope of the formula. *In re Petering et al.* (CCPA 1964) 301

F.2d 676, 133 USPQ 275; *E.I. DuPont de Nemours & Co. v. Ladd, Comr. Pats., et al.* (CADC 1964) 328 F.2d 547, 140 USPQ 297. There can be no anticipation where the reference is so broad that the likelihood of arriving at the claimed composition would be the same as discovering the combination of a safe by an inspection of its dials, *Ex parte Garvey* (POBA 1939) 41 USPQ 583; *Ex parte Starr* (POBA 1938) 44 USPQ 545, nor is anticipation made out by a hindsight selection based on an applicant's disclosure of variables of a broad generic disclosure. *In re Ruschig et al.* (CCPA 1965) 343 F.2d 965, 145 USPQ 274.

As discussed above relative to KALBE '268, the vast number of substituent combinations for formula Ia of KALBE '202 is overwhelming. KALBE '202 also discloses no fewer than 2401 possible combinations for the group R^{1a}, R^{2a}, R^{11a}, and R^{12a} (in paragraphs 62 AND 63 of U.S. equivalent 2004/0043925 A1). Even more possible combinations are disclosed for the group of R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a} and the group of R^{4a}, R^{6a}, R^{8a} and R^{10a}(i.e. paragraphs 64 and 65).

Moreover, KALBE '202, like KALBE '286, fails to disclose or suggest that formula Ia is isolated from a cultured mass of a microorganism having ability to produce the FKI-1033 substance and belonging to the *Verticillium* genus of fungi, as recited in claims 15-19, and that formula Ia has ryanodine binding inhibition activity or is part of a composition having

ryanodine binding inhibition activity, as recited in claims 7, 9, 10 and 13-15.

Thus, the disclosure of KALBE '202 lacks the specificity required for a finding of anticipation, and KALBE '202 does not anticipate claims 1, 7-10 and 13-15, or new claims 16-19.

Therefore, applicants respectfully request that the anticipation rejection be withdrawn.

KALBE '202 would also fail to render obvious the claims, as KALBE '202 fails to even recognize the particular uses for the substance FKI-1033 or the particular microorganism that produces substance FKI-1033 as recited. Thus, there would be no motivation for modifying KALBE '202 so as to limit formula Ia to having a methyl group for R^{1a}, R^{2a}, R^{4a}, R^{6a}, R^{8a}, R^{10a}, R^{11a} and R^{12a} and an n-pentyl group for R^{3a}, R^{5a}, R^{75a} (i.e. R^{7a}) and R^{9a} so as to resemble the recited substance FKI-1033.

Moreover, as discussed above with respect to KALBE '268, KALBE '202 likewise fails to recognize the superior unexpected ectoparasiticidal (anthropodicidal) activity and ryanodine binding inhibition activity of FKI-1033, as compared to the depsipeptides disclosed by KALBE '202 (See the declaration filed along with this amendment).

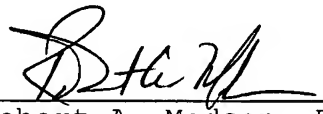
Therefore, applicants believe the claims are neither anticipated nor rendered obvious by KALBE '202.

In view of the forgoing remarks, applicants believe that the present application is in condition for allowance at the time of the next Official Action. Allowance and issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



Robert A. Madsen, Reg. No. 58,543
745 South 23rd Street
Arlington, VA 22202
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

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Appendix:

The Appendix includes the following item:

- Declaration Under Rule 132